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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/540,392	MARKUS, BEIER	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/10/2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18--23, 26-27 and 29-38* is/are pending in the application.

4a) Of the above claim(s) *20-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,19,22,23,26,27 and 29-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Newly submitted claims 18 and 26 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the re—introduced species peptide nucleic acids, proteins, peptides and carbohydrates were withdrawn from consideration in the prosecution of the elected species, nucleic acid. Please see the species election made on 5/14/07. Also, the new claim "oligomeric building blocks" such as di or tri and etc. have not been treated on the merits in the prosecution of the previous claims. The claims prosecuted in the last Office action are drawn to monomers such as nucleic acids as the building blocks.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 18 and 26 with respect to the other non-elected species are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Status of Claims

Claims 18-23, 26-27 and 29-38 are pending.

Claims 20 and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species.

Claims 18(with respect to the elected species, nucleic acids), 19, 22-23, 26(with respect to the elected species), 27 and 29-38 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Written Description Rejection

Claims 18-19, 22-23, 26-27 and 29-38, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record and repeated below.

The specification fails to describe the situ-synthesis of any kind of biopolymer receptor utilizing any building blocks immobilized by any liquid to any given carrier such that a carrier is produced for the determination of analytes. The claim generic method of synthesizing a biopolymer comprises numerous possible biomolecules comprising of numerous receptor building blocks. It is not apparent from the claim generic method whether the liquid containing building blocks to synthesize the receptors into the carrier are of the same or of different kind(s) of biomolecules and/or of the same or different length. The genus claim method provides no characterizing or distinguishing features of one compound/components use in the method. The claim covers numerous undefined components used in the method. It is also not apparent from the specification which carrier has predetermined zones such that only a particular kind of building blocks can attach thereto. The specification lacks adequate written description that would lead a skilled artisan to the genus claim. The specification at e.g., page 5, lines 13-25 provides no more than general statements and/or lists of the building blocks such as the monomers of mononucleotides, amino acids etc., and oligomeric building blocks e.g., di, tri or tetranucleotides or peptides. The specification further discloses that the receptors can be selected from the lists of

nucleic acids such as DNA, RNA, nucleic acid analogs such as peptide nucleic acids (PNA), proteins, peptides and carbohydrates. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the **genus**. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. A listing or definition of every possible surface or target does not constitute a written description of every species in a genus. It would not "reasonably lead" those skilled in the art to any particular species. In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967). Furthermore, there is not a single working example to show that applicants are in possession of a single species of the carrier made, let alone, a genus carrier produced by the claim method. The drawing figures discloses in general terms, not in detail, a method using a specific hapten containing phosphoramidites building block with a diisopropylamino groups and ethoxy derivative. However, it is not readily apparent from the figures the biopolymer receptor that has been produced by the method and more importantly that is used for the

determination of any type of analytes. It is well known in the art that the selection of the right hapten structures is very important to build up an array successfully. Abad et al (J. Agri.Food Chem.) at e.g., page 1486, paragraph bridging col. 1 up to col. 3 states that the critical role generally attributed to immunoassays depends on the fact that the properties of the antibodies are primarily determined by the hapten structure. A strategy that has been sometime successfully included in the coating antibody by hapten to improve sensitivity is irrelevant in other cases. Thus, one may not preempt an unduly large field by the expedient of making broad prophetic statements in the specification and claim unless the accuracy of such statements is sufficiently supported by well-established chemical principles or by sufficient number of examples.

Response to Arguments

Applicant argues that claim 18 has been amended to recite that the carrier has at least 50 biopolymer receptor zones, wherein each zone is different (supported by previous claim 28 and page 6, lines 22-23), the biopolymer receptor building blocks are selected from the group consisting of oligomeric building blocks (supported by page 5, line 15) and building blocks that carry a hapten group (supported by page 9, first

paragraph), and the biopolymeric receptors are synthesized in situ (supported by page 3, lines 17-19 and 37) and are selected from the group consisting of nucleic acids, peptide nucleic acids, proteins, peptides, and carbohydrates (supported by page 5, lines 19-20). In view of the above amendments, applicants contend that the present claims are adequately supported by the written description and request that this rejection be withdrawn.

In reply, the above responses merely provide the support for the newly claimed limitations which is not a detailed description of the genus claim. Please refer above as to the lack of written description rejection of the genus claim. There is not a single working example in the specification to show that applicant has adequately described the (genus) invention.

New Matter Rejection

1. Amended claim 18 which recites "wherein detection of the hapten groups is correlated with the quality and/or the efficiency of the in situ biopolymeric receptor synthesis" as used in the method of producing is not supported in the as-filed specification. Applicant points out support at page 3, lines 25-27. This limitation is applied in the context of a method for

quality control of receptor syntheses, which had been withdrawn from consideration as being drawn to non-elected invention, not to the instant method of making (please see the election made on 5/14/07).

2. The now broad claim “carrier” is not supported by the original disclosure of a specific "microfluidic” carrier, (which has been presently deleted). See e.g., claim 18.

3. The claim to building blocks that carry a hapten is not supported in the as-filed specification. The original disclosure (page 2, lines 9-15) discloses application of the hapten groups to a carrier:

> The object is achieved by a method in which hapten groups are applied to the carrier before the process for synthesizing or/and during one or more steps of the process for synthesizing receptors.

4. Claim 32 recitation of the broad “zones” (which reads on every one of the zones) is not supported by the specific **adjacent** zones (now deleted).

Claim Rejections - 35 USC § 112

Claims 18-19, 22-23, 26-27 and 29-38, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 18 is vague and indefinite as to the synthesis of the building blocks of the receptor i.e., the metes and bounds of the building receptors. It is vague and indefinite whether the building blocks are of the same kind and/or of the same length. It is further vague and indefinite as to how each completely different building block(s) occupied a predetermined zone in the carrier. Claim 18 therefore seems to omit essential elements and/or steps to distinguish e.g., dissimilar building blocks to occupy a zone predetermined for a particular block.

Response to Arguments

Applicant states that claim 18 has been amended to clarify the types of building blocks in the liquid, the particular synthesis method used is not essential as any synthesis method can be used.

In reply, applicant's amendments do not obviate the rejection. The argued different oligomer and/or receptors had

not been treated on the merits and had been withdrawn from consideration as being drawn to the non-elected species. Prosecution on the merits is drawn to the elected species, nucleic acid.

2. Claim 18 is vague and indefinite as to the metes and bounds of the liquid containing building blocks and delivery of said liquid for a particular immobilized block. It is not clear whether the same liquid would be used for any or all kinds of building blocks. It is further vague and indefinite whether in each pass of the liquid the building block is immobilized to the already immobilized block or to another predetermined zone of the carrier. There seems to be some missing element/step or correspondence amongst the steps.

Response to Arguments

Applicant argues that the particular synthesis method used is not essential as any synthesis method can be used.

In reply, the specification recites only microfluidic method i.e., liquid synthesis. There is nothing in the

disclosure except in applicant's arguments that any kind of synthesis can be used.

3. Claim 19 is unclear as to the time specific immobilization i.e., the conditions considered to be appropriate/specific for immobilization.

Response to Arguments

Applicant argues that in view of the disclosure in the present application and the knowledge in the art, one skilled in the art would know the term "time specific" means that the immobilization is carried out at a predetermined point in time. For example, photoactivatable receptor building blocks can be used and activated at a predetermined time. Photoactivatable building blocks are disclosed on page 2, lines 1-5, of the present application.

In reply, the claims do not recite photoactivatable receptor building blocks. Furthermore, it is not the term that is at issue and even so, a "predetermined point in time" is relative. What may be a predetermined time for one may not be for the other.

4. Claim 23 is unclear as to the recitation of closed channels of a carrier. The term “closed” is a relative term the basis or standard by which it is considered close especially in the in -situ synthesis is unclear. The specification does not define said term especially as applied to the general term “microfluidic” carrier.

Response to Arguments

Applicants contend that this term has a generally accepted meaning in the art. This term means that the lumen cannot be accessed except from the inlet and the outlet. In contrast to a "closed channel", an "open channel" can be accessed from the top.

In reply, while the term “closed” is a general term however, its applicability to the instant claim is unclear especially since none of the claim recites the limitation of a lumen.

5. The rejection is withdrawn.

6. The term "high", “specific’ in claim 30”, “adjacent” in claim 32;"selectively" in claim 33; "disposed" in claim 35 are relative terms which render the claims indefinite. These terms

are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Because there are no distinguishing or characterizing features for any of the components use in the method hence each of the terms above are vague and indefinite as to the basis or standard by which the terms are employed. The definition provided in the specification at e.g., page 7, first incomplete paragraph does not point out the terms with particularity. The term "high-affinity interaction" means in this connection that the "interaction between hapten group and binding partner is **sufficiently strong** to enable the incorporation of hapten groups on the carrier to be controlled under particular operating conditions with an appropriate detection reagent". (Emphasis added.)

Response to Arguments

Applicant states that the terms "specific", "adjacent" and "disposed" have been deleted from the claims.

In reply, the deletion of the terms renders the claims more indefinite and vague. For example, if it is not adjacent, then which are the ones considered having no synthesis? How are the

discrete areas identified? Are the haptens applied all over the zones, instead of selectively at the adjacent zone?

Applicants contend that the language "high affinity" is well known in the art. Enclosed with this response are two references which show that this language has an accepted meaning in the art. Applicants also point out pages 6-7 of the present application which discuss "high affinity" interactions.

In reply, the term “high affinity” while generally accepted in the art however, is specifically applied to the case at hand, as evidenced by the newly filed references, and not for the instant method of synthesis.

The newly amended claims are rejected under this statute as follows:

A. Claim 18 is vague and indefinite as to whether an assay (i.e., detection) for the hapten group is being determined or synthesis of the receptor on a carrier. The preamble which recites a method for producing a carrier is at odds with body of the claim of analyzing the hapten on the carrier.

B. Newly amended claim 32 is vague and indefinite and at odds with the newly amended claim 18. Claim 32 recites application of the hapten groups to the complete surface of the carrier. It is further unclear as to the building block carrying a hapten.

Claim Rejections - 35 USC § 102

Claims 18, 19, 22-23, 26-27 and 30-36, as amended, are rejected under 35 U.S.C. 102(e) as being anticipated by Bamdad (USP 7615340) for reasons of record as set forth below.

For claims 18, 19, 22-23, 26-27 and 30-38, Bamdad discloses e.g., the abstract a method of synthesis of members positioned partially or fully in channels in microfluidic systems. The porous members can be assembled and/or disassembled in situ. The porous members can be made such that pores are separated by connections including but a single molecule at one location, allowing for a high level of open area in a very small pore size member. The members can be used to detect analytes qualitatively and/or quantitatively, or to selectively bind and/or release agents on command for a variety of purposes including first blocking, then opening a channel, concentrating analyte

over time followed by release of analyte and detection downstream. Porous members can define valves in multiple-channel systems and, with controlled binding and release of agents at the porous members, these valves can be opened and closed (reads on claim 23) and fluid flow controlled in a multi-channel system. Fluidic systems of the invention can include multiple sensing locations at which different analytes are determined. Systems of the invention provide flexibility for overall microchemical analysis, sequentially, of a variety of agents. Bamdad discloses at e.g., col. 2, lines 44-55, the porous members as preferably biopolymers **that** are assembled in situ within the flow channel so that they become an integral part of the channel. Nanostructures that incorporate particles and biopolymers but do not include ligands that bind a target species are preferred for use as chip-scale filters, such filters can also be disassembled and reconfigured in situ, across interior cross-sections of flow channels. The nano-filters can be anchored to derivatized flow channels via biospecific interactions, such as DNA hybridization and/or biotin-streptavidin binding(hapten, as recited in claim 31). Bamdad discloses at e.g., col. 4, line 43 up to col. 5, line 41 a method that involves passing a fluid through a

porous member and allowing a chemical, biological, or biochemical agent within the fluid to bind to a binding partner of the agent immobilized relative to the porous member.

For claims 28 and 29, Bamdad discloses that the channel can have a cross-sectional dimension of less than about 1000 microns, or less than about 500, 300, 100, or 50 microns in other embodiments.

For claim 32-36, Bamdad discloses a porous member spans a channel, it can span a portion of the channel or can completely span the channel. Where the porous member partially spans the channel, some fluid flowing through the channel will flow through the porous member but other fluid can pass by the porous member and not flow through it. Where the porous member completely spans the channel, any fluid flowing within the channel must pass through the porous member, i.e., the fluid cannot bypass the porous member within the channel.

For claims 30 and 31, Bamdad discloses at e.g., FIGS. 5A and 5B are before and after schematic illustrations illustrating how nanoparticles bearing antibodies and biotin interact with streptavidin and biotinylated dsDNA to form nanostructures that are biospecific.

For claim 31, Bamdad discloses at e.g., col. 8, lines 61-64, affinity tags include streptavidin (in biotin/steptavidin binding) (i.e., hapten). At various locations herein specific affinity tags are described in connection with binding interactions with complementary recognition entity pairs. It is to be understood that the invention involves, in any embodiment employing an affinity tag, a series of individual embodiments each involving selection of any of the affinity tags described herein. Bamdad at col. 17, lines 28-49 discloses the three-dimensional structures constructed of particles and connecting polymers can be constructed across flow channels using a variety of alternative methods to that described above For example, as illustrated in FIGS. 5A and 5B (which illustrate the various components comprising the nanostructure before (FIG. 5A) and after (FIG. 5B) the self-assembly of the interconnected structure) nanoparticle-DNA nanostructures 310 can also be self-assembled by mixing nanoparticles 312, bearing biotin 314, with streptavidin 316 and DNA 318 that has been modified at or near its ends with biotin. This type of nanostructure can readily be attached to flow channels bearing

streptavidin at its surface. See the details of the method in the Examples.

Response to Arguments

Applicant recognizes that Bamdad discloses a microfluidic system which uses interruption of flow through a channel to concentrate or detect analytes for screening. Bamdad describes nano-filters which are assembled in situ in a flow channel. The nano-filters can be differentially modified at different locations to perform a variety of assays on the same sample. But argue that claim 18 has been amended to clarify that the detection of the hapten groups is correlated with the quality and/or the efficiency of the in situ biopolymeric receptor synthesis. Bamdad does not disclose monitoring the synthesis of the biopolymeric receptors using haptens and thus does not anticipate the present claims. While Bamdad does disclose the use of haptens, Bamdad's haptens are not used to monitor the synthesis of the receptors.

In reply, attention is drawn to Bamdad above e.g., FIGS. 5A and 5B. The figures illustrate how nanoparticles bearing antibodies and biotin interact with streptavidin

and biotinylated dsDNA to form nanostructures that are biospecific. Bamdad discloses at e.g., col. 8, lines 61-64, affinity tags include streptavidin (in biotin/streptavidin binding) (i.e., hapten). At various locations herein specific affinity tags are described in connection with binding interactions with complementary recognition entity pairs. It is to be understood that the invention involves, in any embodiment employing an affinity tag, a series of individual embodiments each involving selection of any of the affinity tags described herein.

Thus, the process of Bamdad which is the same as the claimed process steps would inherently disclose that the tags in streptavidin (i.e., hapten) indicate that an efficient synthesis occurred given the biospecific synthesis of the resultant products.

Claim Rejections - 35 USC § 103

Claims 18-19, 22-23 and 25-38, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad in view of Buzby (USP 7220549) for reasons of record as repeated below.

Bamdad is discussed above. Bamdad does not teach the other hapten such as dinitrophenol. However, Buzby

discloses in e.g., col. 2, lines 36-50 primer/target is stabilized on the surface by binding of both the primer and the template to the surface. Binding pairs for use in the invention are any molecular pair that can be bound to a surface and attached to a nucleic acid. Some examples of preferred pairs include biotin/streptavidin, digoxigenin/anti-digoxigenin, and dinitrophenol/anti-dinitrophenol perform well. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use other known hapten groups in the method of Bamdad. One would have a reasonably expectation of success in using other hapten since Buzby teaches the functional equivalence of said hapten groups useful for stabilizing molecular pairs bound on a surface.

Response to Arguments

Applicants point out that neither Buzby or Bamdad disclose a method for producing a carrier wherein hapten groups are applied to the carrier before, during or/and after the synthesis of the biopolymeric receptors to monitor the synthesis of the biopolymeric receptors.

In reply, attention is drawn to the teachings of Bamdad above which illustrate at e.g., FIGS. 5A and 5B (the various components comprising the nanostructure before (FIG. 5A) and after (FIG. 5B) the self-assembly of the interconnected structure. Nanoparticle-DNA nanostructures (310) can also be self-assembled by mixing nanoparticles (312), bearing biotin (314), with streptavidin (i.e., during synthesis, as argued) (316) and DNA (318) that has been modified at or near its ends with biotin. This type of nanostructure can readily be attached to flow channels bearing streptavidin at its surface. See further the details of the method in the Examples.

Claims 18-19, 22-23 and 25-38, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of (WO 0013018)(I) or (WO 0289971)(II) or (WO 02/32567)(III) in view of anyone of Wu et al (7034134) or Gray et al (6555310) or Edwards (6455280) for reasons of record as repeated below.

For claims 18, 19, 22-23, 25-27 and 30-38, Stahler et al (I) discloses throughout the entire document at e.g., page 2 and the claims a method for producing a carrier for the

determination of analytes, comprising: (a) providing a microfluidic carrier, (b) passing liquid with receptor building blocks for synthesizing polymeric receptors over predetermined zones on the carrier, (c) immobilizing the receptor building blocks in said predetermined zones on the carrier and (d) repeating steps (b) and (c) until the desired receptors have been synthesized in the predetermined zones using the receptor building blocks. (U.S. No.7097974 is the national stage entry of WO 0013018, as stated in the Remarks submitted on 6/10/2008.)

See the abstract of each of the Stahler (II) and (III) references. (Please note applicants' remarks made on 6/10/2008, with regards to the corresponding US applications of these two WO Patents).

None of the Stahler references teaches a hapten attached to the carrier. However, Wu discloses throughout the patent at e.g., col. 127, lines 23-27 polypeptides that could be chemically derivatized to attach hapten molecules (e.g., DNP). Wu teaches that due to the availability of monoclonal antibodies specific to such haptens, the protein could be readily purified using immunoprecipation or can be used for other purposes such as for purification via affinity chromatography, functional and/or structural characterization of protein.

Gray et al discloses throughout the patent at e.g., col. 13, line 10 up to col. 14, line 56 a method by comprising contacting library (analyte as claimed) with the receptor immobilized to a solid phase and binding of library members through their tag to the receptor is allowed to reach equilibrium. The complexed receptor and library members are then brought out of solution by addition of a solid phase to which the receptor bears affinity (e.g., an avidin-labelled solid phase can be used to immobilize biotin-labelled receptors). Alternatively, the library can be contacted with receptor in solution and the receptor subsequently immobilized. The concentration of receptor should usually be at or above the Kd of the tag/receptor during solution phase binding so that most displayed tags bind to a receptor at equilibrium. When the receptor-library members are contacted with the solid phase only the library members linked to receptor through at least two displayed tags remain bound to the solid phase following separation of the solid phase from library members in solution. Library members linked to receptor through a single tag are presumably sheared from the solid phase during separation and washing of the solid phase. After removal of unbound library members, bound library members can be dissociated from the receptor and solid phase by a change in ionic strength or pH, or addition of a substance that competes with the tag for binding to the receptor. For example, binding of metal chelate ligands immobilized on agarose and containing Ni.sup.2+ to a hexahistidine sequence is easily reversed by adding imidazole to the solution to compete for binding of the metal chelate ligand. Antibody-peptide binding can often be dissociated by raising the pH to 10.5 or higher.

Edwards discloses throughout the patent at e.g., col. 79,

line 59 up to col. 80, line 40:

Microsequencing may be achieved by the established microsequencing method or by developments or derivatives thereof. Alternative methods include several solid-phase microsequencing techniques. The basic microsequencing protocol...[method] is conducted as a heterogeneous phase assay, in which the primer or the target molecule is immobilized or captured onto a solid support. To simplify

> the primer separation and the terminal nucleotide addition analysis, oligonucleotides are attached to solid supports or are modified in such ways that permit affinity separation as well as polymerase extension. The 5' ends and internal nucleotides of synthetic oligonucleotides can be modified in a number of different ways to permit different affinity separation approaches, e.g., biotinylation. If a single affinity group is used on the oligonucleotides, the oligonucleotides can be separated from the incorporated terminator regent. This eliminates the need of physical or size separation. More than one oligonucleotide can be separated from the terminator reagent and analyzed simultaneously if more than one affinity group is used. This permits the analysis of several nucleic acid species or more nucleic acid sequence information per extension reaction. The affinity group need not be on the priming oligonucleotide but could alternatively be present on the template. For example, immobilization can be carried out via an interaction between biotinylated DNA and streptavidin**-coated** microtitration wells or avidin-coated polystyrene particles. In the same manner, oligonucleotides or templates may be attached to a solid support in a high-density format….Other possible reporter-detection pairs include: ddNTP linked to dinitrophenyl (DNP) and anti-DNP alkaline phosphatase conjugate.. or biotinylated ddNTP and horseradish peroxidase-conjugated streptavidin with o-phenylenediamine as a substrate …….

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use hapten such as biotin or dinitrophenol in the method of anyone of Stahler et al as taught by Wu or Edwards or Gray. Each of Wu, Edwards and Gray teaches the conventionality of using various haptens that binds to different receptors such as nucleic acid or protein. One would have a reasonable expectation of success in using

said hapten as successfully achieved by Edwards or Wu or Gray in purifying various compounds.

Response to Arguments

Applicant states that the claims have been amended to clarify that the haptens are used to monitor the synthesis of the biopolymeric receptors. None of the cited prior art individually or in combination suggests or discloses using haptens in this manner.

In reply, applicant's arguments are not commensurate in scope with the claims. The claims do not recite that haptens are used to monitor the synthesis of the biopolymeric receptors or the steps as to the monitoring of the synthesis using said haptens. Nonetheless, Wu discloses at e.g., col. 127, lines 23-27 polypeptides that could be chemically derivatized to attach hapten molecules (e.g., DNP). Wu teaches that due to the availability of monoclonal antibodies specific to such haptens, the protein could be readily purified using immunoprecipitation (i.e., reads on the claim quality and /or efficiency of the in situ receptor synthesis) or can be used for other purposes such

as for purification via affinity chromatography, functional and/or structural characterization of protein.

Double Patenting

Claims 18-19, 22-23 and 25-38, as amended, are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1, for example, of U.S. Patent No. 7097974('974) in view of anyone of Bamdad or Buzby above for reasons of record as repeated below.

The claim method in the '974 patent differs from the instant claim method in that the '974 does not contain hapten groups in the synthesis of biopolymers. However, Bamdad or Buzby as discussed above teaches the conventionality of attaching in the carrier hapten groups for e.g., stabilizing the biopolymers on the carrier, for example. See further the 103 rejections above.

Response to Arguments

Applicant argues that the claims in U.S. Patent No. 7,097,974 do not suggest or disclose the use of haptens to monitor the synthesis of the biopolymeric receptors. As

discussed above, neither Buzby nor Bamdad disclose a method for producing a carrier wherein hapten groups are applied to the carrier before, during or/and after the synthesis of the biopolymeric receptors to monitor the synthesis of the biopolymeric receptors and thus these references do not cure the deficiencies in U.S. Patent No. 7,097,974.

In reply, since applicants merely present the same arguments under Bamdad and Buzby above hence, the responses above are also applied herein.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 21-22 drawn to a non-elected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/

Primary Examiner, Art Unit 1639